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Alexander Primrose, C.B., LL.D., F.R.C.S. (Eng.), F.R.C.S. (Can.), F.A.C.S., M.B., C.M. (Edin.)

AN APPRECIATION.

By W. B. HENDRY.

It is with affectionate regret that, as the year 1931 passes into history, we have to record the retirement of Professor Alexander Primrose from his position as Dean of Faculty of Medicine of the University of Toronto, and the severance of an intimate association with both undergraduates and Faculty which has extended over a period of forty-two years.

Like the wise men of old, Doctor Primrose came from the East. Born in Pictou, N.S., in 1861, he received his early education in the Pictou Academy, after which he entered a mercantile career in Halifax, in 1880. This was, however, early interrupted by a fortunate accident, which brought him under the professional care of that grand old master of surgery, Dr. John Stewart, whose inspiring tales of Lister diverted the patient's thoughts from commerce

Alexander Primrose, C.B., M.B., C.M.
Edin., F.R.C.S. Eng., F.R.C.S. Can.,
LL.D. Edin, Dal.

and finance. Consequently, after a somewhat prolonged convalescence, the young Alexander set out to conquer the world of medicine, and took his degree, M.B., C.M., from Edinburgh, in 1886. Then followed post graduate work at Middlesex Hospital, London, and Paddington Children's Hospital, after which, in 1889, he returned to Canada, and was at once appointed Demonstrator in Applied Anatomy in the old Toronto School of Medicine at the time of its re-organization. His advancement in this department was rapid. He was made associate professor in 1892 and professor in 1896, which position he held until 1907.

His advancement in Surgery was scarcely less rapid. Appointed associate professor of Clinical Surgery in 1897, he became professor in 1918, which chair he occupied until the end of the past year.

Interested as he has always been in medical education, Dr. Primrose naturally took an active part in the organization and administration of the Faculty of Medicine, of which he was Secretary from 1894 until 1918.

With the outbreak of war, when the University Hospital was being organized, he was among the first to offer his services, and went overseas as Senior Surgeon with that unit. After a strenuous year in the East, he was recalled to Canada, and later was appointed Consultant Surgeon to the Canadian Forces in England, where he served with distinction, and was made a Companion of the Order of the Bath by His Majesty in recognition of his most excellent work.

The post-war period brought many changes to the University. In the Faculty of Medicine old departments were reorganized and new ones created. Expansion was made possible by the gift of the Rockefeller Foundation, and the Faculty required a man of vision, tact and judgment at its head. In Dr. Primrose the Board of Governors found the ideal man, and appointed him Dean in 1920. Since that time the Faculty of Medicine has rapidly developed, until now it ranks second to none on the Continent.

From the very beginning of his regime, Dr. Primrose has whole-heartedly devoted his time and his energy towards furthering the interests of both undergraduate body and Faculty, and by reason of his breadth of vision, kindness of heart and knowledge of human nature, combined with a delicate sense of humour, he has won his way into the hearts of his students and his staff.

Engaged as he has always been in Medical Education, nevertheless he has found time to take an active part in the work of the Canadian Medical Association, of which he is President at the present time, and as Chairman of its Council for many years, he has been in no small degree responsible for its phenomenal growth. He has also done much to promote and foster friendly relations between the University and the profession at large.

His scholastic attainments are universally known, and recently his preeminence as a teacher and a leader in his profession has been recognized by the Universities of Edinburgh and Dalhousie, who have bestowed on him the degree of LL.D. honoris causa. It is sincerely hoped that his name will soon be inscribed in the Golden Book of our own University.

"His life is gentle, and the Elements
So mixed in him that Nature might stand up
And say to all the world, 'This is a Man.'"

EDITORIAL

THE RETIREMENT OF DEAN PRIMROSE.

It was with deep regret that we, the student body, received the announcement of the retirement of Professor Primrose from the office of Dean of the Faculty of Medicine. In his association of 42 years with the Departments of Anatomy and Surgery, he has made many friends, and left a lasting impress on all the students with whom he came in contact. There are many of us whose fathers remember Professor Primrose's polished lectures.

Unfortunate are the succeeding years that they will no longer have the course in Applied Anatomy that his masterly rendering made so unlike the dull reading we find in the texts.

In this issue Professor Hendry tells us about the Dean from a long association, as a student, in the Medical Corps in the Great War, in which they both held the rank of Colonel, and as a member of the Faculty. No one could be more fitted to write this article than Professor Hendry, whom the students join in appreciation of our loss. We only feel that perhaps he has a greater work in the office of President of the Canadian Medical Association — the highest honour that Canadian Medicine can bestow.

A NEW STUDENT JOURNAL.

It is our great pleasure to welcome, this month, a very worthy addition to the small group of medical undergraduate publications on this continent. Following close on the inauguration of Western Ontario's Quarterly, McGill University have undertaken the publishing of a student journal, also a quarterly. It is our sincere wish that both these efforts will meet with every success, and that they will be maintained on the same high standard which they have appointed for themselves.

THEORY IN PRACTICE.

We harbour one type of student who has come to the wrong university for his medical training. One hears him complain about the length of the course, the waste of time on unnecessary subjects, such as chemistry, physics, zoology and history. He wants to "get out and practice," for "how is this stuff going to help you treat patients?" He is evidently a denial to the ambitious hope of those who have planned our curriculum, that 'Varsity graduates be capable of practising the art and the science of medicine with equal authority.

It is remarkable that we graduate without notes on the cure of vomiting or of pain in the abdomen, or of chronic cough. Such complaints as these are, we are taught, merely symptoms of grave and deep-seated disease. We are taught not to do as one recent graduate of another medical school did when a patient telephoned to say he had a stomach-ache and felt "bad" after a party the night before. He prescribed a sedative and repeated it that night when the patient complained of vomiting. The next day, when he examined his patient he found a ruptured appendix.

We are taught enough biochemistry and physiology to know that insulin cannot be taken by mouth; enough physics to know the principle of radium and X-ray therapy and diagnosis; enough fundamental science to be able to grasp opportunities for observation and development in the field of medicine, meaningless to those less firmly grounded. And when a new Banting makes possible a new and valuable treatment, Toronto men should be able to understand the sugar tolerances, glyconeogenesis, acid-base equilibrium and carbohydrate equivalents as they are discussed in the journals. So the much-despised Theory will lead to better Practice.

THE MEDICAL SERVICES.

There was a time when the medical services attracted the picked men of the schools, but the Royal Army Medical Corps is now 20 per cent. below strength. This is no doubt in part due to the low rates of pay, but also to the reaction to military life that has taken place since the war. The Colonial services offer positions of interest and responsibility becoming every year more and more important. Medical science has already turned much of the West Coast of Africa from pestilence-ridden wilds into a reasonably healthy place. It is with such large public health programs as this in which the Colonial medical officer is interested, as well as his routine practice and administrative duties.

The Royal Canadian Army Medical Corps, in keeping with Canada's policy of having only a skeleton army, has a small establishment. The establishment is: 1 Colonel, 6 Lieutenant-Colonels, 7 Majors, 9 Captains and Lieutenants and 2 Quartermasters. At present all these posts are filled.

The monthly pay of a lieutenant on appointment is as follows:—

	Married.	Single.
In quarters	$160	$125
Out of quarters	$200	$180

At the end of one year he is promoted to captain if qualified. From then the promotion is by seniority. The pay of the higher ranks is approximately as follows:—

	Per month.
Captain	$267
Major	$324
Lieutenant-Colonel	$381
Colonel	$434

A pension may be obtained on retiring after twenty years' service, towards which every officer pays 5 per cent. of his pay. It varies from 2-5ths to 7-10ths of the retiring pay, depending on the length of service.

The Naval, Army and Air Force Medical Services in Great Britain have the advantage that their organization is on a large enough scale to allow special training advantages and more varied positions. Post graduate courses in such branches as surgery, medicine, pathology, ophthalmology, etc., are obtainable. The pay is slightly higher than in the Royal Canadian Army Medical Corps, and is pensionable on a similar basis.

The Indian Medical Service at present is sharing in the general conditions of change to which the whole of the Indian State and civil affairs is being subjected. It is retained primarily to meet the needs of the Indian Army. Local governments employ a stated number of Indian Medical Service officers in order to provide European medical attendance for European officers of the Superior Civil Services and their families. Gratuities of £1,000 on retirement after six years' service, or of £2,500 after twelve years' service, together with free return passages for those who no longer desire to remain in the service, are offered to young members of the medical profession. The pay is from £37 a month for a lieutenant, with £11 overseas service, to £168 for a lieutenant-colonel after 25 years' service.

Pensions are based on length of service, and vary from £400 after 17 years' service to £800 after 27 years.

The Colonial Governments employ some 1,200 European medical officers, including 60 women medical officers. In the Colonies there is a great variety of living conditions and pay. Leave is usually granted on very favorable terms when one compares it with the holidays taken by the average man in civil practice.

In most of the services up to one year internship may be applied towards a pension. Militia service also counts half time. The Canadian Officers' Training Corps certificates "A" and "B" also have a definite value in counting towards early seniority and promotion. It is well worth while for the medical student to train in the Officers' Training Corps if he desires to enter any of the services to practice his profession.

The Study of Medicine in the University of Toronto.

By A. PRIMROSE, C.B., M.B., F.R.C.S., LL.D.
Dean of the Faculty of Medicine.

Institutions that have attained an age worthy of note are proud of their antiquity and we are frequently called upon to celebrate centuries of progress in individual cases. The writer was greatly impressed a few years ago when he attended the ceremonies marking the eight hundredth anniversary of the founding of St. Bartholomew's Hospital. As a student he was present at the three hundredth anniversary of the founding of the University of Edinburgh. Such institutions may well take pride in their continuity of useful service over long periods of time. Interesting and valuable traditions, woven into their history, captivate the imagination. These traditions serve as a powerful incentive to the workers therein for loyal and earnest endeavor on their part to enhance the reputation and to perpetuate the fame and prestige of the respective institutions which they serve.

In the Faculty of Medicine of the University of Toronto we have no such historic background. In the year 1887 the Faculty of Medicine, as at present constituted, was established and has attained a high reputation. We are proud of our accomplishment over the short period of little more than two score years.

We in Canada cannot lay claim to great antiquity, Jacques Cartier entered the Baie de Chaleur in 1534 and a year afterward discovered the St. Lawrence River. Thus began two centuries of French rule in Canada, which lasted until the capture of Quebec by Wolfe in 1759; the following year Canada became a British possession. The University of Toronto came into existence in 1827, first known as the University of King's College in the City of York, as Toronto was called at that date. We therefore celebrated our centenary four years ago. A Medical faculty existed for some nine years (1844-1853) and was then abolished; it was not until 1887 that the faculty was reorganized. In the intervening period (1853-1887) proprietory schools taught medicine, sending their students to the University for examination and graduation in medicine. Our medical faculty was therefore founded forty-four years ago. We must acknowledge our extreme youth in the family of British Institutions.

Among individuals the "asset of youth" is recognized as a valuable possession but after all youth is an asset only because it affords opportunity to accumulate wisdom with age and experience. One of our most illustrious British statesmen once remarked, "the arrogance of age must submit to be taught by youth." (Burke). The ideal situation is created when a reciprocal relationship is established between the young and the old to the mutual benefit of both. Our Canadian Universities were primarily founded on the Scotch system of organization. We have perhaps modified and altered our methods to suit our peculiar environment, but the impress and influence of such institutions of learning in the old land are still pre-eminently apparent in Canadian Universities.

Curiously enough there are some advantages in the absence of tradition in an Institution. It is possible that tradition may warp or pervert one's judgment and distort one's vision. A new institution without fixed customs, untrammelled by a slavish regard for authority and possessed of leaders able to initiate policies of a sound and reasonable character, is capable of progress which is sometimes well nigh impossible in an older institution. An extreme conservatism occasionally develops in some of these ancient foundations which results in a certain degree

of stagnation with the development of an antipathy toward new adventure. The history of medicine through the ages teaches us the same lesson. Thus Vesalius (1514-1564)) in the sixteenth century encountered uncompromising opposition from all his contemporaries when he ventured to disprove the doctrine of Galen (130-201) which had held unquestioned authority for fourteen centuries. Vesalius himself was hypnotised by the universal and unqualified acceptance of the teachings of Galen that remained undisputed in his time. It was a severe handicap; it prevented him from making logical and obvious deductions from the accurate observations that he had recorded. It is almost pathetic to note his attempt at times to reconcile his observations with the teachings of Galen in spite of the fact that they were entirely incompatible. Galen taught that the blood passed from one ventricle of the heart to the other ventricle through the septum. Vesalius was unable to find any apertures in the septum but instead of challenging the accuracy of the Galenic doctrine he writes as follows: "The septum of the ventricles, composed as I have said of the thickest substance of the heart, abounds on both sides with little pits impressed in it. Of these pits, none, so far at least as can be perceived, by the senses, penetrate through from the right to the left ventricle, so that we are driven to wonder at the handiwork of the Almighty by means of which the blood sweats from the right to the left ventricle through pasages which escape human vision."

Vesalius regarded Galen with the utmost respect and considered him the greatest physician after Hippocrates, therefore he hesitated to dispute his teaching. Nevertheless he demonstrated beyond all question that Galen was incorrect in many of his descriptions of the bones, the muscles, the brain and other parts of human anatomy. Because of his temerity in thus dethroning Galen he was subjected to such vexatious persecution that he was compelled to leave Padua, the school in which he taught anatomy and where he had accomplished so much to advance scientific truth and to combat error.

In more recent times we find Lister fifty years ago encountering the most bitter antagonism of his colleagues and contemporaries,—leaders of the profession in his day,—who, recognizing the fact that Lister's teaching was revolutionary, exposed him to an attack in which contumely and even ridicule played a part. The hostility exhibited, violent in character, was reminiscent of the persecution to which Vesalius was subjected in the sixteenth century when he too was vilified for his daring to challenge the accepted traditions and doctrines of his time. Lister, like Vesalius, was possessed of a scientific acumen, stimulated by his early training in biology and physiology, which was not shared by his colleagues in the clinical field. He talked in a language which was beyond their power of comprehension. His opponents defended the ancient traditions and refused to abandon their false conception of the etiology of sepsis. As a result the universal acceptance of Lister's teaching was postponed for a quarter of a century. Lister's contribution to surgery has been described as one of the greatest boons ever conferred on humanity. It made possible the wonderful and ever increasing advances in modern surgery, yet his victory over disease was won against the fierce opposition of his contemporaries.

The tragedies of persecution to which Vesalius and Lister were subjected cannot be enacted in our day. This fact becomes apparent when we study the progress of medicine in the last quarter of a century. The medical profession is now instructed in the principles of pure science and the members of that profession are qualified to assess the true value of any scientific discovery in its application to the medical treatment of disease. If, for example, a remedy is suggested for any particular malady, proof of its efficacy must be produced; the clinic and the

laboratory in various parts of the world are utilized to evaluate the claims of the discoverer. The medical profession trained in science, is qualified to accept the verdict intelligently and to act accordingly in the acceptance or rejection of the remedy. The discovery of insulin by Dr. Banting is an example in our own University. The claims made by Dr. Banting and his associates were at once tested in different centres. Scientific proof of the value of insulin in the treatment of diabetes was produced all over the world and this great boon to humanity became immediately available and was utilized by the general profession of medicine who recognized at once the immense value of insulin as proven by scientific methods with which they were familiar. Many other examples may be given, as in the use of the various forms of serum therapy, etc., which have proved of such value in the progress of medicine in recent times.

In recent years great advances have been made in medical science. This has been the more apparent perhaps in the wider application of the methods of pure science to the treatment of the sick at the bedside. The inevitable result has been an increase in the length of the curriculum both in the time devoted to the fundamental sciences and in the final clinical years of study. The difficulty has been to preserve the essential without overburdening the student. The schools of medicine of the old land taught us the paramount value of instruction at the bedside; there the student is required to use his faculties of observation to the limit by a well organized system of clinical teaching. It is interesting to note that John Rutherford was the first to introduce clinical teaching into Edinburgh in 1747-8 (Osler). So called "laboratory tests" are now essential as an additional requirement and it has been difficult to preserve the proper balance between the methods of direct observation employed in physical diagnosis and the use of scientific instruments of precision in the laboratory. In the University of Toronto we have succeeded in preserving the intensive study of the patient at the bedside to an extent equal to the best tradition of clinical instruction in Scottish schools, a tradition which, perhaps more than any other, has enhanced and maintained their reputation for efficient training in medicine.

Far be it from me to disparage a legitimate reverence for tradition or a respect for organized authority. Nevertheless we must examine the tradition to determine whether or not it be worthy. We must challenge authority and determine whether it be true or false. In fact as students, educated in the principles of scientific medicine, we must ever adhere to the scriptural injunction, "Prove all things, hold fast that which is good."

As a matter of fact the evolution of the Faculty of Medicine in recent years has been greatly influenced by the experience and traditions of older institutions and by established authority. On the other hand we have been free to use discrimination and to initiate policies which have been determined upon after the most searching enquiry into the experience of others and having due regard to our own needs and aspirations.

Finally a word may be said regarding our accomplishment. We are told that in the Faculty of Medicine of the University of Toronto, the facilities offered for students in medicine are unsurpassed. Our hospitals and our laboratories have increased in number and efficiency. It is a far cry from the small brick building, in the eastern portion of the city, which in 1887 housed the Toronto School of Medicine, to the series of fine laboratory buildings and hospitals which now constitute the teaching quarters of the Faculty of Medicine of the University of Toronto. This remarkable development has occurred within the life time of the writer who joined the staff as a teacher of anatomy in 1888.

Syphilitic Aortitis and its Complications.

By R. F. NOTT, '32.

Cardiovascular syphilis, with its attending complications, is essentially a disease of the aorta. Warthin has described syphilitic lesions of the heart muscle. However, his work has not been substantiated and the heart appears to be relatively immune to syphilitic infection. This paper will not discuss this problem but will be concerned only with syphilis as it involves the aorta, the aortic valves and the orifices of the coronary arteries.

Etiology.—It is definitely established that the Treponema pallidum is the infecting organism. When the disease is at all advanced it is very difficult to demonstrate it at the site of the lesion but there is frequent association with other syphilitic lesions, history of infection, and a very high percentage of positive Wassermann reactions.

It has been suggested by Klotz that the mode of infection is from the neighboring lymph glands and along the lymphatics which follow the vasa vasorum. The first part of the aorta has a particularly rich lymphatic supply and this corresponds closely to the distribution of the lesion.

Other authors claim a haematogenous entrance of the syphilitic virus as it is common to find an obliterating endarteritis of the vasa vasorum.

Incidence.—Out of 1,024 autopsies at the Presbyterian Hospital, New York, 4.6 per cent. showed the lesions of syphilitic aortitis. Lamb concludes that syphilitic aortitis occurs in from 4 to 7 per cent. of autopsies in a general hospital, that it accounts for from 15 to 25 per cent. of all heart disease, and that it is found in 50 to 75 per cent. of all syphilitics fifteen years after infection.

These figures are for a population in which there is a high percentage of negroes and individuals of low social status. To appreciate the problem as it exists here, they would have to be divided by about ten or more.

This is a disease of middle life, occurring between the period of rheumatic affections and that of atheromatous changes. The average age for the appearance of symptoms is in the neighborhood of forty-seven years.

The disease is much more common in the male sex, about 75 per cent. of cases being in men. Negroes also show a much higher percentage than whites but that may be due to the prevalence of syphilis in that race.

Pathology.—The lesion is quite specific both in the gross and microscopic. It usually begins at the root of the aorta and spreads up and down.

The gross appearance in the later stages shows characteristic healing fibrosis and scarring. The interior of the aorta is seen to be nodular, puckered and thrown into longitudinal folds. This longitudinal wrinkling is characteristic. The intima over the affected parts is usually glistening and pearly although there may be yellow patches of fatty degeneration.

The microscopic appearance is characteristic. In the perivascular lymph spaces of the vasa vasorum of the adventitia and extending for varying distances into the media are collections of lymphocytes and plasma cells. Small miliary gummata are sometimes seen in the adventitia. The most serious process is the destruction of the elastic and muscular fibres of the media. These are replaced by fibrous tissue which is responsible for the scarring seen in the gross. The vasa vasorum penetrate the middle and inner thirds of the media. This is a point of diagnosis. The intima suffers a mild secondary proliferative reaction as a consequence of the inflammation of the outer coats. It shows none of the changes of arteriosclerosis, that is, in uncomplicated cases.

It is to be remembered that syphilitic aortitis is essentially a progressive disease. The fibrous tissue replacement in the wall of the aorta is a poor substitute for the destroyed elastic and muscular fibres. Thus as the replacement continues there is progressive thinning and weakening of the wall. The dilatation following each gush of blood with cardiac systole is not followed by an elastic recoil. Thus there is an ever present tendency to permanent dilatation.

It is thought by many pathologists that the essential lesion is an endarteritis of the vasa vasorum, leading to their obliteration and that the changes seen in the media are due mainly to nutritional disturbance.

In distribution the syhilitic lesion is more comon in the ascending portion. In order of frequency it also occurs in the arch, thoracic aorta and rarely the abdominal aorta. McCallum claims that the proximal parts of the innominate carotid and subclavian arteries may be involved.

Symptoms.—Before there is much involvement of the wall, symptoms are vague and in most cases entirely lacking. However, as the disease progresses two characteristic symptoms become manifest in the majority of cases. The first is substernal oppression or pain which varies in severity from a sense of mild oppression to attacks of pain indistinguishable from severe pain of cardiac origin. It is located beneath the upper part of the sternum or in the precordial region. It is variously described as a feeling of tightness, oppression, constriction or a sense of a heavy weight on the chest. The second is paroxysmal dyspnea. It strikes the patient with startling unexpectedness independent of any exertion. The attacks are usually of short duration, lasting from five to fifteen minutes. They vary in frequency from several a day to only a few during the entire illness. Patients as a rule do not show the customary signs of cardiac failure for months. From first symptoms the length of life in untreated cases is about a year. Expectancy of life may be somewhat more than doubled by treatment.

Signs—depend on the fact that the aorta is less elastic than normal. More of the force of ventricular systole is transmitted peripherally. Thus a forcible systolic thrust over the carotid arteries, unaccompanied by a diastolic collapse as seen in insufficiency, indicates an inelastic aorta. This may also occur in the transverse arch and one can palpate over the manubrium sterni a systolic impulse and a diastolic impact. Syphilis frequently causes elongation of the aorta and upward displacement of the arch. The activity of the vessel can then be felt by deep pressure in the suprasternal notch.

Probably the most valuable sign is an accentuated second aortic sound which is said to be ringing and bell-like in quality. Such a finding in a man between thirty and forty-five years of age, without evidence of arteriosclerosis, hypertension or rheumatic heart disease demands the rigid exclusion of syphilis. In addition a soft systolic murmur may often be heard over the aortic area. It is not transmitted and is probably produced by increased rigidity of the aortic tube.

Diagnosis.—The disease is rarely recognized in its early stages. The blood Wassermann is positive in only about 70 per cent. of cases.

Roentgenological evidence: This is not by any means infallible and the diagnosis should only be made provided the history and clinical findings agree, or at least do not oppose. In brief, significant findings consist of a diffuse or localized dilation associated with a normal sized heart silhouette or a high aorta present in a young individual without previous hypertension. It is said that syphilitic aortitis can be safely diagnosed when there is a localized dilatation associated with increased pulsation demonstrable.

No significant changes in electrocardiographic tracings are found.

Many clinicians believe that clinical diagnosis of syphilitic aortitis, in the

absence of aneurysm and other gross deformities of the aorta cannot safely be established before the advent of aortic insufficiency.

Treatment.—Intensive treatment is desirable and should be given as soon as possible when there are no coronary myocardial or cerebral signs or symptoms.

The patient is first given a six weeks' course of mercury and iodides. This is alternated with a ten weeks' course of not more than 2 gms. of diarsenol per dose. Give these courses two or three times a year. Watch closely for any of the following complications: cardiac failure, nephritis, skin rash or evidence of a damaged liver.

Aortic Insufficiency

This is the first important danger of syphilitic aortitis.

As has been stated above the disease process begins at the root of the aorta and spreads upwards and downwards. In the downward spread it is quite common for it to involve the aortic valves.

Martland believes that the process follows the tissue spaces of least resistance and along perivascular lymph spaces into the aortic cusps rather than following the vessels.

There is pushing apart of the cusps at their attachments by the gummatous and sclerosing process. This widening of the commissure is the earliest sign of aortic regurgitation. A continuation of the process down the attachment of the cusps takes place and often occurs across their free edges. A hyalinized ball-like edge results. The portions of the cusps between the free edges are often remarkably clear of specific sclerosing changes. Martland thinks that many cases of widening of the commissures, the thickening of the edges is largely mechanical in nature and due to the strain produced by the regurgitant blood stream. Sometimes, however the aortic cusps are distorted, thickened, rolled and retracted. Here the valve is irreparably damaged.

Symptoms.—Depend in a large extent upon the ability of the heart to compensate for the lesion. One is impressed, however, by the abruptness of onset of symptoms and the progressive nature of the cardiac failure. The failure of the heart is due to the insuperable burden of the progressive valve lesion. Myocardial damage directly due to the spirochetes is not believed to exist. The changes in the heart are such as are seen in hypertrophy from other causes.

Signs.—There is a change in the systolic murmur which is transmitted up the left border of the sternum and as the cusps become more involved it becomes rough and harsh and transmitted into the vessels of the neck. This murmur is due to the projection of the rigid cusps into the blood stream. Stenosis in the sense of impediment to the flow of blood from the left ventricle is not caused by syphilis.

A diastolic murmur beginning early and best heard down the left border of the sternum, associated with the Corrigan pulse is pathognomonic of aortic regurgitation.

The heart is always enlarged if there is much regurgitation and when regurgitation is marked a very large heart (cor bovinum) is commonly found. The apex impulse is often in the sixth or seventh space and out close to the anterior axillary line.

Roentgenological findings are fairly characteristic. The left median distance is increased, apex is round and elevated from the diaphragm. Heart is in the transverse position, giving the so-called shoe shape. The aortic shadow is broad.

In uncomplicated cases the electrocardiogram shows markedly abnormal left axis deviation.

The pulse is very high as the disease progresses.

In about 50 per cent of the cases death is due to congestive heart failure. Sudden death is common, occurring from acute cardiac dilatation or

closure of the orifices of the coronary arteries.

Treatment.—Here intensive specific treatment is of little value and distinctly dangerous. Rest, digitalis and the orthodox treatment for cardiac failure are to be employed.

Aneurysm.

Aneurysm of the ascending portion and the arch only, will be considered.

The production of aneurysm is but a further step in the weakening aortic wall. As pointed out above the tendency in syphilitic aortitis is to permanent dilatation. The situation and type of aneurysm is dependent on the site of the disease process. If the process is fairly well confined to one part of the aorta there is the formation of cylindrical or fusiform type. The more common form, the sacculated aneurysm, originates from a localized area of weakness on one side of the aortic wall.

At autopsy a great many specimens of aortic aneurysm will show little or no involvement of the aortic valve. The production of aneurysm is more likely to occur if the aortic valve is competent, and the maintenance of a high diastolic pressure against the weakened aortic wall is possible.

The endothelial lining of the aneurysmal sac is soon lost in places. Thrombus forms with organization of a typical lamination. This has often been a protective influence, as many layers of a laminated clot may act as a tampon.

Martland claims that the heart in aortic aneurysm is not usually enlarged unless there is coexisting regurgitation.

Symptoms.—Many of the signs and symptoms of aortic aneurysm depend upon pressure and erosion on neighboring structures. They are: **Pain,** which is most common. It may be constant and boring in character because of erosion of bone; may be intermittent and neuralgic on account of irritation of nerve fibres. It is less apt to be severe if the aneurysm involves the ascending arch. **Dyspnea,** apart from that on exertion and the paroxysmal type, may be due to constriction of the trachea, main bronchus or the lung itself. **Cough** may be an early symptom due to pressure on the trachea. **Hoarseness,** more commonly in aneurysm of the arch because of pressure on the left recurrent laryngeal nerve. **Dysphagia** may be due to direct pressure on the oesophagus.

It is to be remembered that in addition to the above symptoms any or all of the symptoms noted in syphilitic aortitis may be present.

Signs.—Strip the patient and have him in a good light.

Inspection: Note any inequality of the pupils due to pressure on the sympathetics. Also any pulsation, systolic in time, sharply circumscribed or diffuse in the second or third interspace to the left or right of the sternum, over the manubrium, in the episternal notch or posteriorly in the left scapular region or below the angle of the scapula.

Palpitation: On the area overlying an aneurysm a distinct heaving may be noted. If the chest has been eroded the impulse often has an expansile quality. A systolic thrill is felt in many instances. There may be tenderness on pressure over the sternum. Tracheal tug is present in aneurysms of the arch when the sac becomes adherent to the trachea.

Percussion: Dullness on percussion is perhaps the most important sign. The normal dullness over the sternum is converted to flatness, and diminished resonance is frequently elicited in the first and second interspaces, to the right or left of the sternum.

Auscultation: The most constant and characteristic sign is a loud ringing second sound.

Whenever aneurysm is suspected a fluoroscopic examination should be made.

Treatment.—The treatment here is essentially the same as in syphilitic aortitis. For the aneurysm itself, in the early stages at least, much may be accomplished by rest. Get the patient to

go to bed for periods of ten or twelve weeks at a time. The diet should be adequate but not excessive. Alcohol and tobacco should be interdicted. Pain may be treated by ice-caps or sedatives and paroxysms by nitrites.

Coronary Stenosis and Atresia.

It is said that one in four cases of syphilis of the aorta show some narrowing of the coronary orifices. In the adaptation of the heart to such conditions the element of time is a very important factor. There is gradual formation of a collateral circulation from one coronary artery to the other and the Thebesian vessels.

In a series of deaths occurring from syphilitic aortitis stenosis or atresia of the coronary ostia account for about 30 per cent. It comprises about 15 per cent. of the sudden deaths from syphilis of the aorta.

In 1925 Von Glahn observed that often one or both coronaries may have their origin above the sinuses of Valsalva. As syphilitic aortitis usually starts in the portion of the aorta above a base line drawn through the upper limits of the attachments of the aortic cusps, coronary arteries which are congenitally situated above this are especially liable to scarring of their ostia, while those arising normally in the sinuses often escape encroachment.

Syphilitic coronary disease is practically limited to a narrowing or atresia of their orifices by the lesion in the aortic wall. The right coronary seems to be more liable to narrowing than the left.

Diagnosis.—It is here that anginal pains are most liable to occur. This is to be expected on account of the impaired nutrition of the walls of the heart. They will be typically of a cardiac nature in that they will appear with physical exertion and be relieved by rest. Along with this look for a history of syphilis and clinical, or laboratory, evidence of syphilitic aortitis.

Treatment.—Antiluetic treatment is as a rule contraindicated. If decided upon great care must be taken to prepare such a patient properly for arsenicals. Too early an injection may be followed by a Herxheimer reaction with oedema of the coronary orifices and sudden death or a severe attack of cardiac pain and all its consequences. Intensive treatment may result in too rapid healing of the syphilitic process, leaving a stenotic scar. Thus the patient may be in a worse condition than before (therapeutic paradox of Stokes).

Rest and attention to the general health is probably the best line of treatment in these cases.

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ERRATUM.

We regret the fact that the bibliography for the article on "Common Infections of the Hand," by G. M. Bastedo, M.A., M.D., and Kent Harrison, M.D., was omitted from the December issue of the Journal. It is as follows:

Kanavel—Infections of the Hand.
Nelson—Loose Leaf Surgery.
Gray's Anatomy.
Babcock's Surgery.
J. A. Couch—Lectures to VIth Year and Personal Communication.

THIRD YEAR REPRESENTATIVE.

Applications for **third year editorial representative** will be received until Jan. 20, 1932. Address to the Editor, University of Toronto Medical Journal, Anatomy Bldg.

A Brief Sketch of the Origin and Development of the Indian Medical Service.

By MAJOR G. SHANKS, B.A., M.D. (McGILL), I.M.S.
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The history of the Indian Medical Service goes back to the "Spacious times of great Elizabeth," for its beginnings were associated with those of the East India Company, the Charter of which is dated the 31st of December, 1600. In December, 1600, the first fleet of the company sailed for the East. In each of its four ships were "surgeons two and a barber." So, oddly enough, the first Medical Officers in the employment of the East India Company were surgeons on board ship.

About the same time, in addition to these Company Medical Officers, other medical men from Europe began to find employment as physicians and surgeons at the courts of various Indian and other Eastern Rulers.

Among the first of these were George Strachan, a Scotsman, who served in Arabia with the Arab Emir Feiad in 1615-18; Francis Bernier, a Frenchman, who was a surgeon with Shah Jeban's son, Dara Shitoob, with Aurongzeb and others. He returned to Europe through Persia in 1670, or thereabouts, after having been in India for ten years; and Nicholas Manucci, a Venetian, who remained in India from 1655 to the time of his death in 1717. (Age then 79).

The first Surgeon General to the East India Company was appointed in 1614—the incumbent named being John Woodall, a surgeon to St. Bartholomew's Hospital. It is, by the way, an interesting fact in this connection that many Bart's men have been officers in the Indian Medical Service. It was almost the case, it is said, that, some years ago, only Bart's men could become Professors at the Medical College in Calcutta. Woodall remained in London but had to supervise the Medical Services on the ships going East and the equipment.

The first Company Factory established in Western India was that at Surat in what is now the Bombay Presidency. It was started in 1612-13, and by 1617 four more were in operation—at Broach, Barhanpur, Ahmedabad, and Agra. Surgeons were appointed to all of these. The men appointed, not very highly qualified, and not generally of the best type, held very low rank in the Company's service.

The first factories on the East Coast were those at Nizampatam in Madras, founded in 1611, and at Patna, started on the 3rd of July, 1620. I have been in the latter, which is now used for printing by the Government of Bihar and Orissa, of which Patnā is the capital city. It developed into an extensive series of well constructed buildings, which, as seen now, give one the impression of considerable defensive strength. They are surrounded by a moat and wall, and through the wall there is an outlet to the mighty Ganges by which river it stands. The river at this point has a width of a mile and a half. This Patna factory, by the way, was the scene of more than one massacre by the Indians. One occurred in 1763.

Throughout the seventeenth century trading went on at various factories in Bombay, Madras and Bengal. Their sites were changed from time to time on account of hostile actions by various deputy rulers. Attached to these trading factories were medical men some of whom have left good reputations, and others decidedly bad ones.

During the first half of the 18th century the company remained simply a trading corporation with three chief settlements independent of each other, at Bombay, Madras, and Calcutta, and a few factories up country. The factory at Calcutta was first begun in 1686.

This was only a temporary settlement as it had to be vacated once or twice during the next four years. Its final foundation dates from August 1690. I would here emphasize the fact that the development of the great ports of India — Calcutta, Bombay, Madras, and Karachi — has been entirely due to British enterprise. In 1868 there was nothing at Intanuti where now stands the fine city of Calcutta, with its population of 1,500,000, its fine business and public buildings, and its splendid jute factories. During this period — the 17th and 18th centuries — there was a steady increase in the business activities of the Company, in the importance, size and number of the factory settlements, and, as a result, in the number of medical men engaged.

Among the most famous—the most famous I should say—of the surgeons during the 18th century was John Zephaniah Holwell, the hero of the Black Hole of Calcutta. He was a surgeon until 1750, when he went home for two years, returning as a Covenanted Civilian Official (not medical). He was a man of great energy and ability. He had some ideas of sanitary improvement — probably rare enough at that time in Calcutta—for on the 12th of May, 1755, he asked leave to repair and enclose the great tank, and to prohibit the washing of people and horses therein. This was the large tank, known as the Lal Dighi, or red tank, around which Dalhousie Square has been built; then, and for more than a century afterwards, it afforded the best drinking water available in Calcutta! Holwell was a Member of Council in Calcutta in June, 1756, when the Nawab of Bengal, Siraj-ud-Daulah captured the city. The surrender was followed, as is well known, by the tragedy of the Black Hole.

During the siege Drake, the Governor, deserted the garrison — an episode almost without parallel in English history—and Holwell by general consent took over the conduct of the defence. He survived, was taken prisoner, and sent to Murshidabad in chains. When released he went home but returned about two years later. In 1759 he erected, at his own expense, a monument to the victims of the Black Hole, about the spot where their bodies had been thrown into the ditch surrounding the Fort. This monument was pulled down about 1821 but a fac-simile was erected and unveiled by Lord Curzon in 1902.

The actual foundation of the Indian Medical Service as such occurred with effect from the 1st of January, 1764. Orders were passed in the Fort William Gazette of the 20th of October, 1763, by which the individual medical officers, then serving in the Bengal Presidency, were combined into a regular medical establishment, with fixed grades and definite rules for promotion from grade to grade. Warren Hastings was present at the meeting at which this decision was made. This constituted the Bengal Medical Service. Its strength was fixed at forty — twelve full surgeons and twenty-eight mates. The Madras and Bombay Medical Services appear to have come into existence at about the same time as the Bengal Service. But no orders regarding the formal Constitution of these services appear in the Consultations, Military or Civil, or in the letters of the Court of Directors, of either Madras or Bombay, in the years 1763 and 1764.

The strength of the service rapidly increased. While at first only civil appointments were made, soon the need for military surgeons was experienced, as fighting occurred in both Madras and Bengal. In 1766 the Medical Service was divided into two branches, Military and Civil. These were at first separate. This arrangement was found to be impracticable. The matter was finally arranged by a decision that officers of the I.M.S. are all primarily military officers, that those in Civil employ are only lent for civil duty, in which they form a reserve for the army, and that they are all liable to recall to military duty at any time. The maximum total strength reached 819 in 1861 but has receded progressively

from this since that date. It was 770 in 1913 and is now considerably less.

Passing over without comment a considerable period of time during which the Service carried on throughout India, we reach the year 1857, when the Mutiny broke out. This was practically confined to the Bengal army, which, by the way, was not composed of Bengalis—the Indian Army has had a very few Bengalis or Madrassis as Sepoys. In the Mutiny a number of I.M.S. officers lost their lives, and for the most part, these belonged to the Bengal Service. They were 28 in number, of whom 9 perished at Cawnpore.

After the mutiny the Government of India was transferred from the Company to the Crown. This momentous change was proclaimed in India by Her Majesty, through the Viceroy, at Allahabad, on the 1st of November, 1858. By this Act the Military and Naval Services of the East India Company became those of the Crown. The Indian Army was amalgamated with the British Army by a General Order dated the 10th of April, 1861, when Royal Commissions were conferred upon the combatant officers of the Company's Army. By clause 44 of the Warrant of the 7th November, 1864, the officers of the I.M.S. also received Royal Commissions.

Schultz's Syndrome—Agranulocytosis.

By S. J. BOCHNER, B.A., '32.

Definition.

A symptom complex of sudden onset, occurring more usually in females of middle age, but not uncommonly at other ages or in males; characterized by symptoms of acute sepsis, and associated with necrotic ulceration of the mucosal surfaces, more usually of the oronasopharynx, together with a profound leucopenia and marked reduction to complete absence of granulocytic elements in the circulating blood and bone marrow, with little or no change in the erythropoietic or thrombocytic tissues.

History.

Türk in 1908 had reported extreme leucopenia with infection, but not till Werner Shultz, in 1922, gave a more thorough description, with case studies, was general interest aroused. Beatrice Lovett gave the first American report in 1924. There followed innumerable reports in both Germany and America, and of recent years reports have appeared, in almost every medical journal, in rapidly increasing frequency. The result has been confusion, rather than definition, with application of the term to conditions of recognizable etiological entities, such as benzol poisoning, aplastic anaemias and aleukemias.

Shultz described it under the heading of "Das Neue Krankheitsbild Agranulozytose." Friedmann coined the term "Agranulocytic Angina," as suggestive of a definite association. Kastlin, in America, supported this view. Hueber, in a review, suggests "Agranulocytosis" alone, or "Septic Agranulocytosis," as suggestive of the probable etiology. Magner prefers the group heading "Schultz's Syndrome."

Clinical History.

Hueber points out that in Friedmann's review of forty-nine cases, twenty-five gave histories of preceding infectious processes, or trauma, and that fifteen further cases gave histories of indefinite illness, as fatigue, weakness, and at times malaise, for periods of a month to a year. The acute symptoms come on suddenly, with chills, fever and prostration. Sore throat is usually present at the onset,

as a diffuse pharyngitis. Within twenty-four to forty-eight hours the patient complains of marked dysphagia and examination reveals necrotic ulcerative stomatitis. The acute duration is short. Of the forty-nine cases catalogued by Hueber, more than half were dead in seven days. No chronic form has been reported, though several cases of acute recurrences are recorded by Hamburger, Friedmann and others.

Angina, though common, does not appear in all cases. Conner, Margolis, Birkeland and Sharp reviewed fourteen cases, presenting four with no angina and three others with doubtful angina. They observed, as did many others, that the "features of the condition were essentially identical, with angina and without." The tonsils are most usually involved, but the necrotic processes are by no means limited. Spreading widely, they are found on the lips and tongue, as in the larynx and oesophagus. In the intestines there is produced an enteritis and diarrhoea, commonly giving rise to the suspicion of typhoid fever. Similar necrotic processes have frequently been reported in the skin, appearing as small ulcers, spontaneously as septic emboli, or as the result of minor injuries. Kaznelson reported the necrosis of the whole fingertip, which had been pricked to obtain a drop of blood for a smear.

Schultz described icterus as a feature. Kastlin reported icterus in 58% of his forty-three cases. In many of these it was slight. Hueber looks upon it as terminal, and as a manifestation of general toxaemia.

The Blood Picture.

The startling feature is the marked leucopenia. In a series of seventy-four cases accepted as such, by Hueber, and having complete blood analyses, the highest white count was in a case of Friedmann's, 4,600 per cu. mm. On the other hand, Schultz was unable to find any cells in the counting chamber in two of his cases.

The greatest polymorphonuclear count observed was 40%. The others were very much lower, many showing 0%. Those cells that were found, in many cases, showed signs of degeneration.

Eosinophiles appeared in many cases —in some definitely increased. Hueber observed that a persistent eosinophilia was present in those cases going on to apparent recovery. Minot noted the phenomenon in cases of recurrent agranulocytosis.

In only fifteen of Hueber's series was there an absolute increase of lymphocytes. The cells that appeared were largely adult forms. Rutledge, Hansen-Pruss and Thayer report an early increase of lympocytes with the appearance of immature forms in the circulation, in cases of recurrences closely observed.

The large monocytes and endothelials were present in increased numbers in many of the cases. Hueber interprets this as a reticulo-endothelial response to sepsis. Heck reports four cases with definite monocytosis, three of which recovered. However, he reports another case with 60% monocytes which ended fatally.

The platelet count was normal. Hueber considers the many cases in the literature under the heading of Agranulocytosis, showing reduced platelets and hemorrhagic diatheses as not belonging to this group. In this he is supported by most authorities.

The red blood cells are remarkably normal in appearance and numbers. Only fifteen cases of Hueber's series showed a red count of under four million. Frank points out that the erythropoietic system is the most resistant of the blood forming tissues to external noxious agents, and Hueber considers the short course of the illness as the reason for the apparent freedom of the red cells.

Bacteriology.

Various organisms have been cultured from the lesions and to some extent from the blood stream; staphylococci, streptococci hemolyticus and

non-hemolyticus pneumococci, B. diphtheriae and Vincent's organisms are among the principal findings. There is no uniformity in the various reports or in the reports of the same observer.

Pathology.

Extensive necrotic ulcerations is the prominent feature, not only in the oronasopharynx, but throughout the gastro-intestinal tract. The distribution in the small intestine simulates that of typhoid ulceration. These areas are fairly well demarcated. There are masses of bacteria evident throughout the necrotic tissue. The remarkable feature is the lack of cellular reaction, with but a few lymphocytes and an occasional multinucleated and degenerated polymorphonuclear in evidence.

The regional lymph glands were found to be enlarged in most cases, yet in only two of Hueber's series did suppuration develop, and in both only during convalescence. In no case was there a generalized lymph gland enlargement. The microscopic picture is not characteristic.

The spleen is usually enlarged to some extent, but markedly so in very few. The pulp is toxic in character, swollen and dark red in colour. The cells of the myeloid series are practically absent, as demonstrated by the oxydase method. There is some increase of the plasma cells, and in some cases of the cells of the reticulo-endothelial system. Various large irregular cells were noted by some observers. These are looked upon as degenerated myeloid cells, even though they do not take the oxydase reaction.

The liver shows cloudy swelling and fatty degeneration. There is considerable variation of the picture, but in no case is there any significent cellular reaction or infiltration.

The kidneys showed similar toxic changes. In some cases an actual nephritis was noted.

The bladder mucosa suffers as do other mucous surfaces. Friedmann reported a case of extensive necrotic ulceration.

Haemorrhagic consolidation, infarction, gangrene, pulmonary thrombosis are the more common findings in the lungs. Sharp reports a case of pneumonic consolidation of the lower two-thirds of both lungs. The alveoli were filled with masses of blood cells, fibrin and bacteria. There were many large endothelial cells, some of which were packed with blood pigment, but there was no cellular reaction.

The bone marrow showed some degree of erythroblastic hyperplasia in many cases. In no case was there any aplasia evident. Similarly, the megalokaryocyte content appeared normal. The myeloid tissue, on the other hand, showed marked aplasia. Only occasional myeloid cells could be demonstrated by the oxydase reaction. Occasionally large, poorly staining, irregular cells were reported, similar to those appearing in the spleen, and here, too, they were considered to be degenerated myeloid cells.

The reticulo-endothelial structures were in some cases appreciably increased.

Hueber looks upon external extravasation and hemorrhages as not a part of the agranulocytosis picture. Such extravasations or petechiae are, however, fairly commonly present throughout the viscera. Hueber considers them due to septic thrombosis. They are commonly noted as points of hemorrhagic necrosis appearing in the subserous surfaces and fairly commonly throughout the lung.

Differential Diagnosis.

1. The Acute Aleukemias. — The picture presented is very similar, as sudden onset, fever and prostration, with ulcerating necrotic processes of the mucous membranes, together with the leukopenia. There is, however, usually associated frequent gross and petechial haemorrhages, with, as a rule, thrombocytopenia. In most cases there is some increase of abnormal myeloblastic cells in the circulation. At times the oxy-

dase reaction is necessary to differentiate them, and it should therefore be done as a routine in all these cases. Considerable anaemia is usually in evidence. Finally, the autopsy shows signs of myeloid or lymphoid metaplasia, and in the bone marrow a reduction of the megalokaryocytes.

2. Massive Acute Sepsis.—Cases of severe sepsis are not uncommonly associated with leukopenia and some degree of hypogranulocytosis, even to agranulocytosis. It is well known that such a reaction is indicative of a poor prognosis. Petechial haemorrhages are frequent, but by no means the rule. Increasing anaemia is usually encountered. Leukopenia is characteristic of some acute infections, such as malaria, influenza and typhoid fever, to a degree relative to the severity of the condition. An increased monocytic count is another similar feature. A clear cut differentiation can therefore not possibly be made in many of the cases.

3. Infectious Mononucleosis. — The clinical picture closely resembles that of agranulocytosis, though in a more moderate form. Commonly there is a sore throat, though not often going on to severe ulceration. There is some fever and general malaise. The illness subsides in two or three weeks. The blood picture shows an absolute lymphocytosis, with occasionally an absolute decrease of granulocytes. The white count is usually well above the normal. Zadek reports a case of apparently typical infectious mononucleosis which was followed by a reactionary picture, simulating agranulocytosis. The white blood count fell to 900 per cu. mm., with 32% polymorphonuclears. There was a positive staphylococcic blood culture.

4. Aplastic Anaemia.—Aplastic anaemia is occasionally associated with necrotic lesions, and a septic course similar in many respects to agranulocytosis. The marked anaemia, haemorrhages, deficiency of platelets and general bone marrow aplasia establish the diagnosis.

5. Diphtheria.—Most cases are first taken for diphtheria. Bacteriological study and blood findings, however, soon decide the question.

6. Chemical Poisoning (Benzol) — Chemicals, such as benzol and its derivatives (arsphenamine), produce a marked leukopenia with often an entire aplasia of the myeloblastic elements. This is not uncommonly associated with necrotic ulcerations and a septic clinical picture, resembling agranulocytosis. However, the history of contact, haemorrhages, which are common, and rapidly developing anaemia, help in establishing a diagnosis.

Etiology.

Characteristic cases have been reported from all parts of the worlld, and at all seasons. The frequency is greater in females, with about 25% of reported cases in males. It occurs at all ages, but most commonly at the period of 40 to 55. Although there is considerable uniformity of opinion as to diagnosis and description, there is a great deal of controversy as to the underlying cause. Several theories have been propounded.

1. Specific Infection.—It is very unlikely that there is a specific causative agent, with so great a variation in the bacterial findings. A virus, Hueber points out, would not be effected by radiation as a means of therapy.

2. Endocrine Disturbance. — Friedmann suggested an endocrine disturbance as the basis for the haematological upset, on the grounds that most cases occur in females at or about the climacteric. Minot, in discussing the case of Rutledge, Hanson-Pruss and Thayer, suggests that the similarity of the recurrences to the cyclic character of menstruation raises the question of altered endocrine function as the cause of the periodic depression of the bone marrow, with the resultant lowered resistance to infection.

Rutledge, Hanson-Pruss and Thayer report a case of recurrent Agranulocytosis throughout the life of a male, 20 years of age. The "attacks" were characterized by

fever of 3 - 10 days' duration, increasing to 104 - 105° F., furunculosis, anginal sore throat and diarrhoea, with a characteristic blood picture. These recurred at irrigular periods, during early childhood, but later showed a remarkably regular three week interval. When examined by Dr. Thayer at the age of 19, his voice was just changing as of a boy at puberty, hair on the face were sparse, and pubic hairs were transversely arranged. No further physical abnormalities were found. The external genitalia appeared normal.

3. Imperfect Myeloblastic System. — Hamburger argues that the primary disorder rests in the depressed function of granulocytopoiesis, as an inherently imperfect system, and so favours the clinical identity of these cases. He points to cases that have been diagnosed by the house officers at his hospital (the Johns Hopkins) upon the clinical picture alone. None of his patients suffered any obvious infection prior to the development of a sore throat; some had been fatigued for some time, and he suggests that, had a leukocyte count been done at that time, a reduction would have been found. Leuchtenberger reports two cases in which the blood picture had been present for months prior to the clinical disease. Batten argues along the same lines, in that cases show "a strong familiar likeness," and that the clinical picture appears sufficiently clear to deserve a descriptive name. Thompson, writing in Nelson's System of Medicine, essentially agrees with Batten, and would establish it as a distinct disease entity. Nordgren, presenting cases of recurrance, looks upon the agranulocytosis as the essential feature, lowering the resistance such that a comparatively mild infection takes on malignant proportions. He explains the common association of necroses of the gastro-intestinal tract as due to the frequent minor trauma, and the abundant more or less virulent bacteria normally there present.

4. Sepsis With An Altered Reaction. Hueber in his investigations shows a high frequency of preceding infection, acute or chronic, in the cases of his series. He believes that the bone marrow has been so depressed as to be unable to efficiently react to another invasion, thus giving rise to a vicious circle, and terminating in death due to the overwhelming sepsis. The negative blood cultures so often procured he explains as due to lack of persistence. Considering the rapid course and early death of the patient, he argues that the time is not sufficient to procure positive blood cultures in all cases. Kastlin similarly regards the condition as an "inconstant individual reaction to sepsis." He reports two cases with an initial leukocytosis, which within a day or two fell to 1-2000 per cu. mm., with later a white count of 100, and 10% polymorphs. Piney looks upon Glandular fever, Mononucleosis and Agranulocytosis as different forms of the same process. Felderman aptly sums up his argument by saying that "when a patient dies of an Angina, it is termed Agranulocytosis, and when the patient recovers it is just a simple Vincent's case."

Treatment.

Minot recommended whole pituitary therapy in Dr. Thayer's case. There was little or no evident effect.

Friedmann introduced Roentgen irradiation of the long bones. He reports excellent results with early treatment. In 15 non-fulminating cases he procured 13 recoveries. The method has, however, not been as successful in other hands.

Reznicoff introduced nucleotide therapy. Adenine sulphate or guanine hydrochloride, given intravenously into rabbits, produced marked granulocytosis, without fever or other cellular disturbances. He reports successful treatment of a case using .5gms. adenine sulphate daily. The patient, however, also received daily transfusions. The Squibb people have placed a "leukocytic extract" on the market which may be of some value in these conditions.

Frequent small transfusions have frequently been used, and undoubtedly have their place.

Powdered arsphenamine, or, as a glycerine paste, locally applied, has been recommended. The doubtful relation of Vincent's spirella throws some question upon its value. Early and vigorous local treatment is urged by many, using frequent, mild antiseptic irrigations.

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Burns.

By A. H. JEFFREY, B.A., '32.

Reviewing the sixty-one cases of recent thermal burns admitted to the Hospital for Sick Children in the year 1930, the important agents responsible for the lesion were: (1) Scalds, 51 per cent. of cases with one death. (2) Falling into a receptacle of hot water, 18 per cent. of cases with two deaths. (3) Clothes on fire, 11 per cent. of cases with three deaths. (4) Hot solids, 13 per cent. of cases with no deaths. In these figures one is struck with the high mortality when the clothes have caught fire or the patient has fallen into a receptacle of water, in which cases extensive burns are to be expected. Autopsy records agree with this finding and also indicate the danger of gasoline burns.

Such figures do not include the extensive out-patient work. The number of brush burns, which are essentially friction burns, is not given credit above, as they rarely require admittance on account of the burn. However, we are dealing with an exceedingly common condition which is usually superficial and quite similar pathologically. Fifty per cent. of burns occur under five years of age, with a steadily decreasing incidence up till mid-life, when the industrial occupations add their toll.

Pathology.

A. Local. When the wound is cleansed it is usually possible to estimate both the extent and depth of the burn—two factors which allow us to judge the immediate and eventual prognosis. Dupuytren classified burns into six degrees, namely:

1. An erythema of the skin. Oedema may occur which lasts at the most two days.

2. Vesication.—The epidermal cells have undergone a true coagulation necrosis, and fluid passes from the papillae of the corium into the epidermal layers to give rise to vesicles. It may exist at any level above the basal cell layer, is due to the action of a toxin

on the capillaries, and is usually considered to be plasma.

3. In the third degree there is destruction of the epidermis and the tips of the papillary processes of the corium, with, however, the tips of the interpapillary processes remaining intact. On cleansing the wound thoroughly preparatory to treatment, the papillae which have been injured will appear as definite red points on a light background, though in areas where the burn has almost obliterated the epidermis, one may see white spots, representing the islands of basal cells occuring in the interpillary downgrowths, on a red background. This observation is of prime importance to make at the time of cleansing as it affects the eventual prognosis so radically. The formation of new skin takes from two to four weeks and the new skin may have a pink tinge for several months, but usually results in a normal coloured skin with all the structural elements of true skin, and undergoes no contraction.

4. Involves destruction of the entire epidermis and usually the corium. The burn is brownish and dry if produced by dry heat, otherwise white, and insensible; may be cracked with an outflow of fat from the subcutaneous tissues. The formation of granulation tissue is not marked until the eschar has been removed. From the margin a thin layer of epithelium grows in at the rate of one-eighth of an inch per week. The new epithelium will be thin, smooth and shiny, inelastic and very apt to undergo contraction from scar tissue beneath.

5. Encroachment on muscles. The burn is deeper, firm and immobile. Considerable disability may follow the cure.

6. Carbonization.—Rarely seen except in the fingers and toes of those insensitive are paralysed.

B. General.—Of the eighteen autopsies since the advent of the present treatment, five cases died in the first twenty-four hours, and twelve cases died in the first four days. The remaining six had some degree of infection beneath the eschar. Two of the latter died from septicaemia alone at the end of one month. On post-mortem there is no constant finding, but certain lesions occur with sufficient frequency to merit consideration.

1. Fatty degeneration of the liver was present in seven of the eighteen cases. However, of the twelve who died in the first few days only three of these showed any fatty degeneration of the lobule, suggesting that it takes a longer time for the toxins to affect the liver cells. We might presume that in all serious cases there is a destructive action of the toxin, as, of the six who died after four days' time, four showed central lobular degeneration, and the remaining two suffered from less serious burns, but succumbed with a definite septicaemia. In no cases was jaundice observed.

2. Kidneys—six cases showed degeneration in the glomerulous or convoluted tubules. These were insufficient to cause renal impairment and bore no definite time interval with regard to the accident.

3. Suprarenals.—Two cases of haemorrhage into both cortex and medulla, and two into the medulla alone occurred. Thrombosis of the veins was noted in two of these cases.

4. Gastro-Intestinal Lesions.—Duodenal ulcer was noted in three cases at a distance of one to five centimeters below the pylorus and thus not in relation to the ampulla. One of these cases showed thrombosis of the blood vessels in the vicinity combined with thrombosis in the suprarenals. Small petechiae were seen in the stomach once, and in the lower ileum once. However, several clinical cases of haematemisis failed to show any anatomical lesion responsible for the same.

5. Haemorrhagic findings in addition to the above occurred as follows: subserous—four cases, intrathymic—two cases, and single cases of haemorrhage into the floor of the lateral ventricle, myocardium and kidney cortex.

6. Lymph glands.—Necrosis of the

centre of the lobule characteristic of toxic conditions was noted in three cases, in only one of which it was generalized.

7. Two cases of fairly extensive burns showed general lymphoid hyperplasia and were dead within forty-eight hours.

8. Congestion of various organs is to be expected with the circulatory failure in most cases.

The results of these autopsies convey only one anatomical lesion which may be responsible for death—haemorrhage into the adrenals. However, they suggest the presence of a substance toxic to the body cells generally. Subsequent discussion will emphasize the importance of functional rather than visible morphological changes in the body cells due to the toxin.

Systemic Features.

The elaboration of a toxin at the sight of the lesion is amply proven by the results of treatment by surgical debridement and experimental crossed circulation. The toxin is carried by the red cells and is likely a proteose. The identification of the toxin may have some value from the viewpoint of antitoxin therapy in the future, but the changes in the composition of the blood are the factors worthy of attention from the standpoint of treatment. The first thing is a concentration of the blood indicated by decreased plasma volume. The sodium chloride of both whole blood and plasma undergoes rapid changes. Davidson has done the most recent work along this line. He found no true relation between blood volume and plasma chlorides. In extensive burns the blood concentration was at a maximum on the first determination (time interval not stated), whereas the plasma chloride fell rapidly the first few days, then more gradually to reach the low point at the tenth day when the blood concentration had returned to normal. Suppression of urinary chloride paralleled decreased plasma chloride. The reduction could not be accounted for by diet, vomiting or transudation. A low blood chloride persisted as long as the devitalized (tanned) tissue was present, but on separation there was a rapid restoration of plasma chloride with an outpouring in the urine. Evidently there is a storage of sodium chloride throughout the body analagous to that seen in lobar pneumonia.

Davidson found that when the sodium chloride of the plasma was low there was little change from normal in the carbon dioxide combining power. As no alkalis were given we should expect an increase in plasma proteins to maintain the osmotic pressure. Such did not take place and there was a negative nitrogen balance, most marked from the fourth to the sixth day. A similarity in the blood chemistry of burns and acute intestinal obstruction is noticeable. In both conditions plasma appears to leave the vascular system.

Hyperglycaemia is usual in the toxic stage, but rarely leads to glyosuria. Urinary suppression is the rule, and albumin is most marked in the severe cases.

Underhill made an interesting observation re the permeability of the capillaries beneath the lesion. From the second to the sixteenth hour there increased permeability from the lumen out for diffusible colloids, at which time a lethal dose of strychnine on the surface will give no toxic symptoms. This one-way permeability disappears after about the sixteenth hour.

Clinical Picture.

Only a small percentage of patients showed a considerable degree of primary shock. In all such the immediate prognosis is less favourable.

The depth of the burn is not so important as the extent. There were few cases of deeper burns on which to judge. However, of the thirteen cases which have died in the last two years, but one of these had only a second degree burn. Fourth degree burns are

usually extensive. All cases involving more than forty per cent. of the body surface succumbed in 1930; but there is also the individual factor, viz.:

Case 1. Age 14 months. Child received small second to third degree burn on the lateral side of the leg one evening. It was dressed in the outpatient department with tannic acid next morning, at which time the child was apparently in good health. No untoward signs were noted till that evening, when twitching of the limbs with drowsiness and fever occurred. She was admitted with a temperature of 103 degrees. In one hour child was quite toxic, pulse 144, respirations 68 and vomiting. Convulsed and vomited blood in twenty hours' time. Exsanguination transfusion failed to rally the child and she died within twenty-four hours of admission.

In the average case of moderate burns on admission the child is suffering considerably, not crying unduly, face is flushed, pulse accelerated slightly, and temperature elevated one or more degrees. Under favourable circumstances the temperature will fall to normal in a variable number of days up to one week, during which time there is no evidence of circulatory failure. The child is quite comfortable within two hours of when treatment is started.

The unfavourable case will be admitted in a state of shock which usually responds to a transfusion more or less favourably. Under proper treatment the child becomes fairly comfortable. The temperature may become 103 degrees plus, pulse running, and respirations fast. Vomiting occurs in about twenty-four hours. The child becomes drowsy, toxic, cyanosed, and twitching of the muscles occurs. The vomitus becomes brownish in colour due to blood, and child succumbs in convulsions in the first forty-eight hours.

Vomiting and convulsions are ominous signs in these cases. In the sixty-one cases of 1930 vomiting occurred in all but one of these resulting fatally, and in but two cases which rallied.

There is yet a third type of case where the child recovers well from shock and appears to be progressing well for the first few days when the signs of toxaemia begin to appear. For example:

Case 2. Age 6 years. Clothes caught fire one hour previously. Admitted badly shocked, pulse not palpable, apex 140 and semi-conscious. Three-quarters of the body involved in third to fourth degree burns. Transfused and continuous saline instituted. Patient much improved second day. Towards the end of the third day twitchings of the muscles occurred. Temperature rose to 103 degrees the fourth day and child became irrational, dying the eighth day. Autopsy showed that tannic acid fixation did not extend down to the deepest dead epithelial cells. Also in this case there was necrosis of the right inguinal lymph gland, fatty degeneration of the

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liver and kidney tubules, petechiae in the stomach and an ulcer in the duodenum. These lesions of toxicity were numerically greater than the lesions in all other cases complicated by shock or sepsis.

Thus we have three causes of death to consider:

1. Those dying in the first three days from shock plus toxaemia. This was the most common cause.

2. Toxaemia alone. There were only two deaths that fell in this group in the thirteen deaths in the last two years or the eighteen autopsy records since 1926. Was probably a common cause before the present treatment.

3. All infected wounds do not die, but in extensive wounds there is a liability to infection with consequent exhaustion. One-third of the deaths fall into this group.

Treatment.

A. General.—The patient should be transferred to a hospital if possible should the burn be extensive or the general condition warrant such procedure. Preparatory to cleansing morphia should be given, which may be combined with atropine. When shock is present cleansing should be delayed, and a direct transfusion is indicated with a continuous intravenous saline on return to the ward. It is advisable to cleanse the wound surface and begin the tanning before twenty-four hours' time; as symptoms of toxaemia begin to appear, saline and fluids are pushed either per os or intravenously. From recent studies it appears that a transfusion is indicated in moderate toxaemia in order to maintain the proteins. All cases so treated in the series showed a moderate recuperation, even if merely temporarily, following this procedure. The exsanguination transfusion is being discarded now, as the results are often disappointing. It is the custom to give alkalis in the form of sodium citrate wth glucose and orange juice.

A couple of hours after the tanning is started the child is quite comfortable and there is no need for sedative. Depending on the extent of the burn a burn-bed is indicated—which is merely a sterile-covered bed maintained at a temperature of 80 degrees by incandescent lights. Such is advisable till out of danger of shock, when it should be discarded on account of the moisture lost.

B. Local.—The requirements of the treatment are to stop pain, prevent absorption of toxins and loss of body fluids, insure asepsis, prevent scar formation, and form a scaffold for the growth of young epitheial cells over the denuded area. The various forms of treatment are:

1. Use of oils, salves, etc. Their only use is analgesic.

2. Biochemical—Proteoses require a slightly acid medium for their activity, and the alkaline medium suppresses this, preventing autolysis of the eschar. Compresses of saturated sodium bicarbonate are used; the action is analgesic and previous to the introduction of tannic acid this was one of the best methods.

3. Protective paraffin dressings—should be discarded.

4. Fixation—principal of healing under a crust making use of antiseptic drugs with a dessicating and fixing action on the cells.

(a) Absolute alcohol—continuous saturation over gauze dressing. Produces minimal scar.

(b) Aluminium acetate—tannic acid is to be preferred.

(c) Picric acid—one per cent. solution in five per cent. alcohol. Disadvantages are toxic effects due to absorption and yellow stain.

(d) Tannic acid.—Tannic acid is a cheap amorphous powder readily soluble in water to give an amber-coloured solution; and forming a stable compound with the divitalized body cells without affecting living tissues in the least. For instance it can be sprayed about the eyes without danger. The preferable strength has not been determined for deepest penetrability. A

ten per cent. solution in sterile water is used here though the powder itself may be found as suitable in the future. Tannic acid has all the requirements of the ideal treatment to certain degrees. Studies have shown that there is little danger of death from toxaemia alone. The problem is to prevent infection and treat the shock. The infection is combated by methodical and thorough cleansing of the wound. Sterile towels are draped about the patient, and with the usual sterile technique the wound is thoroughly scrubbed with gasolene and gauze. A much greater area of skin than appears devitalized can be removed, and forceps may be used to pare off the last margins.

Tannic acid is given by spray when a burn-bed is used, spraying every twenty minutes. Otherwise compresses are used which should be kept well saturated with the solution. When the tan is moderately formed, paint the edges with mercurochrome. In twenty-four to forty-eight hours the tanning is complete, and if no infection is present, all dressings may be removed, and patient allowed to go about as usual if general condition permits. In case of infection drainage should be instituted.

The tannic acid treatment is so far ahead of all other forms that there should never be reason for the general practitioner not having a supply on hand. Compresses of this solution may be applied under all usual conditions.

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The Etiology and Pathology of Tabes Dorsalis and General Paresis.

By A. L. RICE, '32.

Syphilis of the nervous system may be classified as:—

A. Cerebral Syphilis.
1. Syphilitic Meningitis.
2. Cerebro-spinal syphilis.
3. Syphilitic Endarteritis.
4. Gummatous Tumours.

B. Parasyphilis.
1. General Paresis.
2. Tabes Dorsalis.
3. Tabes Paresis.

Etiology.

In 1850 Tabes Dorsalis was recognized and worked out as a clinical entity by Todd. A little later Romberg classified the important signs and co-related the symptoms with disease of the dorsal columns. A little later the clinical features and pathology were further analysed and clarified by Duchene.

At about the same period the foundations of our knowledge of General Paresis were laid by Bayle and Calmeil, and it soon came to be recognized by many as a definite entity.

Neither of these conditions were associated with syphilis until early in the second half of the 19th century. A summary of the knowledge of syphilis of the nervous system prior to this time gives:—

The first reference to the pathology of syphilis of the brain was made by the Father of Pathology, Morgagni, in 1761. In 1790 the eminent John Hunter taught that syphilis, gonorrhoea and soft chancre were all manifestations of the same disease, and that neither viscera, brain or spinal cord could be affected. This erroneous impression was partially removed by Lallemonde in 1835, when he demonstrated a series of syphilitic brains. In 1858 Virchow

worked and presented the pathology of Gummatosis, which showed that a gumma in the brain was possible. In 1874 Heubner described syphilitic endarteritis which he found in all parts of the body, including cerebral vessels. Thus in 1880 it was fairly well established that gross syphilitic lesions could and did exist in the nervous system.

About 1883 the noted neurologists, Fournier and Erb, first thought of the possibility of Locomotor Ataxia and General Paralysis of the Insane as being forms of syphilis, so they carefully went into the histories of a large series of tabetics and paretics. They found a definite history of primary syphilitic lesions in 80% of cases, and of the remaining 20% they could not exclude the possibility of previous infection. While this epochal work did not provide definite proof, it is highly important, since it provided the stimulus for other workers to attack the problem by laboratory methods, which later conclusively proved the theory.

Considerable discussion and not a little confusion then arose as to the forms of syphilis of the nervous system, as locomotor ataxia and general paralysis could not be put into any of the stages of syphilis. Fournier (1886) again clarified the problem by showing that these diseases were not tertiary syphilis since gummata were not present, and the symptoms were entirely different as to form and time of appearance. He describes them as post-syphilitic or parasyphilis, which term remains to-day. Mott gave the classification which appears at the beginning of this article.

Such was the state of our knowledge up to the beginning of the 20th century. In 1906 Wasserman, using Bordet's complement fixation phenomena (1901) developed the now famous serological test for syphilis. Using this, it was soon found that a positive reaction was obtainable in the blood or cerebrospinal fluid, or both, in 75-85% of cases of Tabes-dorsalis and 85-90% of General Paresis.

In 1905 Schaudin and Hoffman established the Treponema Pallidum as the etiological agent of syphilis, and in 1913 Noguchi and Moore forged the final link in the etiological chain by demonstrating these organisms in the spinal cord of tabetics and in the brains of paretics, although they could not show the spirochete in every case. Other workers have since shown that the spirochetes are present in such small numbers that localization is exceedingly difficult.

Although previous syphilitic infection is the prime factor, other factors such as ill-health, malnutrition, lowered resistance, chronic alcoholism, trauma, physical fatigue, mental fatigue, and similar conditions all play an important part in the development of tabes dorsalis and general paresis.

Pathological Anatomy of Tabes Dorsalis.

In the gross the cord appears to be smaller than normal, and the soft membranes thickened and opaque. The dorsal nerve roots are wasted and grey, while the ventral roots are normal. There are no marked changes on the surface of the brain except that the pia covering the base may be somewhat opaque.

The parts of the spinal cord which show lesions in Tabes are the afferent fibres forming the dorsal roots, whose cell stations are in the spinal ganglia. As these fibres enter the cord a small portion turn laterally to form Lissauer's tract, the fibres of which run upwards and downwards for a few segments, and terminate in the grey matter of the dorsal horns. The majority of the fibres pass medially and then turn upwards, forming the fasciculi gracilis or cuneatus, depending upon the level taken, and ending in the nuclei gracilis or cuneatus. These are proprioceptive fibres from muscles, tendons and joints conveying the sense of position in space. The fibres conveying tactile, thermal and painful sensations are part of the same roots, but as these cross at various levels, their changes are more difficult to trace in their upward course.

The pathological changes are best studied by examining stained sections of the cord, beginning below and taking succeedingly higher sections.

In the lumbo-sacral enlargement the root entry zones are pale, degenerated and atrophied. The fibres forming the most lateral parts of Lissauer's tract and the fasciculus gracilis are degenerated. Those fibres of the medial parts which enter lower down are not affected. This picture is seen all through the lumbar enlargement. As one reaches the thoracic region no degeneration is seen in the root entry zones, but the degenerated portion of tract begun lower down is again seen, since normally the fibres are pushed more and more medially; one sees a section of degeneration with normal fibres on either side. In the lower cervical enlargement this degenerated tract is, of course, present, but, in addition, degeneration of the root entry zones again appears, and as one examines higher sections the degenerated fibres from these roots are seen, this time passing into the fasciculus cuneatus. Thus a section just below the nuclei gracilis and cuneatus shows alternate layers of normal and degenerated fibres.

From the above it is seen that degeneration begins in the root entry zones of the lumbar and cervical enlargements, and passes upwards to the nuclei. These changes correspond to the clinical picture of signs and symptoms in the legs and arms chiefly. In very severe cases the major part of both fasciculi are degenerated. In these severe cases the glial tissue is proliferated to replace destroyed fibres. The process may extend into the medulla, involving the spinal root of the trigeminal nerve, thus accounting for rare cases with trigeminal symptoms. The nuclei of the vagus, hypoglossal and auditory nerves may be involved in rare cases. Much more frequently the optic nerves show degeneration.

Other changes considered by many authors to be secondary to the above are:—

The cells of the spinal root ganglia of the lumbo-sacral and cervical enlargements show degeneration. The posterior horn cells, particularly of Clarke's columns, show degeneration. Rarely in severe and advanced cases the anterior horn cells may be degenerated, giving muscular atropy. In fact, in rare cases practically any part of the cord may be degenerated.

There are, however, cases with severe symptoms and but little to be found at autopsy, and conversely cases with few symptoms but with marked pathology.

Pathological Anatomy of General Paresis.

Here the brain cortex is involved primarily and the other tissues secondarily. The frontal and parietal lobes show the chief changes, those of the frontal being the first to appear and showing the most marked changes.

Macroscopic Appearance.—A haemorrhagic or hypertrophic pachymeningitis with a thin exudate is seen in about one-half of the cases. There is always a chronic leptomeningitis, the pia being thickened, opaque and adherent to the cortex. The fluid in the subdural and subarachnoid spaces is increased. In the latter it is often enclosed in small cyst-like foci — an external hydrocephalus. An internal hydrocephalus may also be present, the ventricles being distended with fluid. In the fourth ventricle a granular ependyma may often be seen. The weight of the brain is diminished and the convolutions of the frontal and parietal lobes, especially the frontal, are flattened and atrophied with wide gaping sulci. This feature is almost pathognomonic.

Microscopic Appearance. — The pia is moderately thickened and is infiltrated with plasma cells and lymphocytes. This is especially noticeable in that forming the Virchow-Robin spaces. The normal arrangement of the cells of the cortex is distorted on account of atrophy and degeneration of the nerve cells. These are replaced

by glial tissue, which is evidenced by the appearance of numerous astrocytes. All the layers of cortical cells are affected to a greater or less degree, but the degeneration is most marked in the most peripheral layers. The association fibres — tangential fibres and outer lines of Baillarger, are degenerated. The neuroglia is greatly increased and shows active proliferation throughout the whole cortex, especially about the blood vessels. Moderately large rod-shaped cells (Nissl's Rod Cells) are scattered throughout. These cells are a form of glial tissue and are peculiar to General Paresis.

All the blood vessels show either proliferative, mild inflamatory or degenerative changes, more particularly those of the cortex. There is a perivascular infiltration of plasma cells and lymphocytes, some of which may be seen in any of the coats of the vessels. The endothelium and adventitia are proliferated, the lymph spaces of the latter being dilated. These vessels may show regenerative changes in favorable cases as time goes on. There is some doubt about as to whether the cortical cell degeneration is primary or secondary to the blood vessel changes — both are always present.

While these changes are most marked in frontal and parietal lobes, scattered degenerative changes may be found in the cerebellum, basal ganglia, corpora quadrigemina and the nuclei of cranial nerves. Pachecho (Russia) found spirochetes in general paretic brains much more commonly in the frontal lobes than in the parietal, rarely in the meninges and never around blood vessels.

The Nature of the Changes.

It is now considered by most writers that the changes in tabes dorsalis and general paresis are similar in nature but different in location, but the real nature of such changes is still unsettled. The various hypotheses may be divided into two groups:—

The first group regard the changes in the meninges and blood vessels to be primary, and those of the dorsal roots or of cortex secondary. Redlich and Obersteiner believe the roots to become constricted by a neuritis and a thickening of the pia at the point where they pass through to enter the cord. (The ring of Obersteiner). Nageotte's views are somewhat similar, but he places the origin more distally, where the roots pass through the dura. Hassin, working under Jakob, has shown that there is an infiltrative and proliferative changes in the pia arachnoid at the Ring of Obersteiner which invades the perineural spaces, causing stasis of the cerebrospinal fluid from the subarachnoid spaces. While these changes have been found in a few cases by other workers, they have not been generally confirmed. They do not explain the almost invariable escape of the ventral roots, and they do not account for the varying clinical picture. That the disease begins at the Ring of Obersteiner is generally conceded, however.

The other group regards the degeneration of the nervous tissue to be primary, due to the action of a toxin. Hauptman believes that the spirochete acting as a foreign body elaborates a proteolytic ferment, which is especially prone to attack nervous tissue. This may explain the wide variability of the clinical picture, since toxins are often selective, picking out certain tissues either by functional or anatomical arrangement. Orr and Rows have shown by animal experimentation that toxins may spread along peri-neural lymph spaces of peripheral nerves and enter the cord through the dorsal roots. Using staphylococcus aureus, they were able to produce degeneration in the medullated fibres at the root entry zones and dorsal columns very similar to that seen in tabes dorsalis. They also show that a secondary proliferative and infiltrative meningitis followed.

The question is not settled, but the latter view appears to be the most widely held.

Pathogenesis.

A question which is still causing much discussion is whether or not parasyphilis is caused by the same type of spirochete as in the more ordinary forms of syphilis. Some of the evidence in favour of a special strain of spirochete is:—

Nonne and Strümpel (France) have observed, firstly, there is much higher proportion of tabes dorsalis and general paresis following mild cases of syphilis which did not go beyond the first stage. Secondly, the more frequent occurrance of conjugal tabes and paresis, i.e., where both husband and wife were affected. They found this in 10 - 20% of cases where ordinarily not more than 5% should develop parasyphilis, inferring that the husband and wife received the same strain of spirochete. Similarly, in a big proportion of cases, juvenile tabetics have tabetic parents.

Guillain, Perisson, Thevenard and Marie also make similar observations. Marie described an instance where both parents and two children all developed general paresis.

Levaditi and his co-workers (1920) undertook to obtain experimental proof as to the existence of this special strain. They took a strain of spirochete from a chancre and another from nervous tissue of a general paretic and inoculated each into the eyebrows of two series of monkeys. The strain of the general parentic did not produce lesions of any kind after months of waiting. The strain from the chancre produced definite syphilitic lesions from which spirochetes were recovered about a month after inoculation. Similar results were obtained using higher apes. Then they injected some of the strain from the general paretic into the testicles of monkeys and apes, producing small mild localized gummata. They concluded that there were two distinct types, which they named Neurotropic and Dermatropic.

Frederick Eberson of California, in discussing this work, points out—

First, the dermatropic type used by Levaditi was not taken directly from the chancre, but had been passed through rabbits for twelve months, which may have materially changed its virulence. Secondly, to be conclusive, both types should be injected into nervous tissues, which should give in the one case some form of syphilitic lesion and in the other some evidence of parasyphilitic manifestation. He contends that the environment of the spirochete accounts for all the differences in characteristics. In other words, spirochetes having lived in nerve tissue, would show entirely different characteristics than would the same spirochetes had they been located elsewhere.

McIntosh and Fildes (England) made the observations that in as far as the blood vessel changes are concerned, the histological picture is the same for any type of syphilis or parasyphilis, viz.: perivascular lymphocyte and plasma cell infiltration. Furthermore, Ravout has shown that there are the same meningeal irritation and cerebro-spinal fluid changes in 60% of all cases of syphilis having no nervous system symptoms, and that such changes occur within two or three years after infection.

These observations would indicate that there is no special strain of spirochete necessarily, but that parasyphilis is an end stage of a common syphilitic infection.

It is almost a universal observation that insufficient or incorrect treatment of the original syphilis will cause parasyphilis to occur in a much higher proportion of cases. Seemingly this sort of treatment is sufficient to destroy most of the spirochetes, but some remain, possibly having acquired an increased resistance, and remain latent for long periods. Why these organisms become pushed into the nervous system is still an unanswered question.

There are many clinical observations published for and against the theory of a special strain of spirochete, and the question must remain open.

A theory has been advanced by Edinger as to why some develop tabes

and some general paresis following syphilitic infection. He assumes that the toxin of syphilis attacks the whole nervous system, lowering its resistance to the extent that while it can carry on perfectly under ordinary conditions, if subjected to undue strain or fatigued in any way, it can no longer maintain its metabolic equilibrium, and consequently degenerates. Thus, persons using their brains chiefly will be the ones to develop general paresis; persons using their legs a great deal (soldiers, etc.), will develop tabes dorsalis affecting the legs; persons using their arms (blacksmiths, etc.) will show tabetic symptoms in their arms chiefly, and so on. It is a frequent clinical observation that a mental strain or an emotional shock often precedes both of these conditions.

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A SPECIFIC FOR ADDISON'S DISEASE.

The last decade has been an active one in the realm of therapeutics. In 1923, insulin revolutionized the treatment of diabetes; in 1926, Minot and Murphy showed that liver was specific for pernicious anaemia — not to mention the less widely advertized treatments such as malaria for general paresis.

One of the latest of these great advances seems now assured. Swingle and Pfiffner reported the preparation of an active suprarenal cortex hormone in March, 1930. This has been found to be a specific for Addison's Disease, and the latest report on its use is very optimistic, in spite of some cases terminating fatally while still under treatment. When it is realized that the cost of the extract as now prepared is enormous (as was the case for insulin for a short period), and that not enough is obtainable at present to give a theoretically adequate dose; and also that Addison's disease is usually due to tuberculosis — 100% success under such circumstances is beyond the dreams of ambition. 1 c.c. of this extract is obtainable from two steers, and in animal experimentation 1 c.c. per kilogram was the dose worked out to maintain adrenalcotomized animals. Their success in a majority of cases thus far has resulted from 3 to 10 c.c. intravenously per day instead of 90 c.c. per day. The cessation of nausea and vomiting, reappearance of appetite, diminution of pigmentation, and return of a sense of physical and mental vigour with some increase in blood pressure, are all apparent within 24 to 72 hours after treatment is begun.

The results in the treatment of anorexia nervosa, asthma, myasthenia gravis, diffuse myositis and other diseases more or less related to adrenal cortex have been negative — so that Swingle and Pfiffner's fluid appears to be a specific for Addison's disease alone.

That the extract is not obtainable here at present, and is prohibitive in cost as well, should not dampen the expectations that another disease will soon be under the control of medical science.

The Clinical Application of the Sex Hormones.

G. L. MORGAN SMITH, M.A., '34.

Recently a subject that has been of great interest to the gynaecologist, if one can judge by the frequency of its appearance in the literature, is the clinical application of the sex hormones. The physiologist and the biological chemist, and, in many cases, the clinician himself, acting in the rôle of research worker, have occupied themselves in the preparation and testing of the active principles of the ovary and the anterior pituitary gland. One of the most successful of these researches is the Ashheim-Zondek test for pregnancy. Other results that have not yet proved their merit are in the direction of the therapeutic use of the sex hormones. From recent work, however, it seems that there is great hope that the intelligent use of potent extracts will be of value to the physician.

Ovarian transplants and emulsions were early known to restore the uterus and vagina to their normal state after the atrophy of castration. The first experimenters worked under the great difficulty of having no satisfactory test for the hormones of the ovary. It was not until the vaginal smear technique of Stockard and Papanicolau was adapted by Allen and Doisey to the assay of oestrin that this was overcome. Satisfactory tests have also been devised for the hormone or hormones of the corpus luteum, in lengthening of the oestrus cycle in guinea pigs, and relaxing the pubic ligament of the pocket gopher. This means that active ovarian preparations can be assayed by a standard technique on animals and the potency determined with no great variation, a great step towards the clinical application of any product.

The Reproductive Cycle.

From puberty to the menopause, rats and mice have a regular sex cycle which consists of a gradual building up of the mucosa of the uterus and vagina, until these organs are almost double their resting size, culminating in the period of heat, or oestrus. At this period of maximal enlargement of the genital tract the mature ovarian follicle bursts and discharges its contained ovum, which proceeds down the Fallopian Tubes. If the ovum is ferilized, it becomes implanted in the uterus, which still increases in size and shows changes in the type of its mucosa. This post-ovulatory condition is spoken of as the luteal phase, governed as it seems to be by the corpus luteum. The initial growth of the genital tract is termed the follicular phase, initiated by the production of oestrin, which is formed in the follicle or interstitial tissue simultaneously with the follicular growth.

Should the ovum not become fertilized, the oestrus upbuilding of the genital tract is rapidly followed by a shredding of the epithelial cells and the appearance of leukocytes in large numbers, and the resting size of the uterus and vagina is regained. This oestrus cycle of enlargement of the genital tract, ovulation and appearance of certain physical symptoms, such as willingness to mate, re-occurs every 4 or 5 days in rats and mice, and is interrupted only by pregnancy from the time of puberty to senescence.

In some animals in which there are only a limited number of cycles a year, a definite period of pseudopregnancy follows oestrus, if pregnancy does not intervene. For a period varying in different species from a few days to almost the length of a full-term pregnancy, there is a luteal phase that is indistinguishable from pregnancy, except for the actual presence of a placenta. Breast changes take place, so that often a slight secretion is noted. Moreover, irritation of the uterine mucous membrane will lead to the forma-

tion of a decidua, a plaenta-like growth. This phase has been shown to be due to the hormone of the corpus luteum, and can be terminated by removal of the yellow body.

If the ovaries are removed from a female mammal all sexual activity ceases. The injection of oestrin causes the typical oestrus changes in the genital tract similar to natural heat even as regards the mating instinct. It is these changes detected by the alteration in the cell structure of the vagina of the castrated female rat that constitute the most reliable test for oestrin.

The question now arises: *What is the relation, if any, between human menstruation and heat in the lower mammals?* On the surface it would seem that they might be quite analogous, but this is not so. Ovulation in the human takes place about midway in the cycle, and it is this period that must be identified with heat in the lower mammals. It must be noted that there is no special period of sexual desire in the human female as there is in the lower mammals. The corpus luteum effect is seen in the post-ovulation phase, and may be responsible for the premenstrual breast changes, as well as the proliferation of the glandular type of uterine mucosa. That the secretion of oestrin still occurs up to the beginning of the menstrual flow has been shown by Frank. Evidently the most efficient action of the luteal hormone is dependent on a preliminary follicular phase, as has been demonstrated by Weichert.

In the event of pregnancy intervening, the luteal phase is dominant until the ovum is firmly implanted and placentation takes place. The ovaries do not appear to be then so essential for continued foetal life, possibly because of the assumption by the placenta of endocrine elaboration. Oestrin, and the luteal hormone, as well as the sex factors of the pituitary gland are found in the blood of pregnancy in quite high concentration.

If fertilization of the ovum does not occur, menstruation results. This consists of a shredding of the mucosa down to the basal layer, with considerable resulting bleeding. It represents the discarding of an elaborate system for nutrition of the egg, for which there is no need, and occurs coincidently with a decrease in the amount of oestrin in the blood, as well as with the degeneration of the yellow body. This is the normal menstrual cycle.

Allen has shown that bleeding will occur in ovariectomized monkeys as a result of administered oestrin, but only after the injections have ceased. He also describes two different types of menstruation in monkeys, each showing characteristic histological pictures in the uterine mucosa. From this it appears that human menstruation may be simply the post-oestrus condition of lower mammals and termination of pseudopregnancy telescoped into one period, with excessive shredding of the mucosa and bleeding in the discarding of unnecessary tissue. In cases where there is no ovulation, and hence no formation of the yellow body, the bleeding is entirely of the post-oestrus type, similar to that occurring in spayed monkeys receiving no oestrin.

The anterior pituitary gland has at least two sex-hormones, termed prolan A and prolan B by Aschheim and Zondek. These act through the ovary, and have no effect on the castrate. Prolan A causes follicular maturation and ovulation, with the resulting changes in the genital tract due to the oestrin liberated by the maturing ovary. Prolan B causes luteinization alone. Thus the synergistic action of Prolan A and B will cause a normal sex cycle. Any disorder of the prolan producing cells of the anterior pituitary gland will be reflected in the ovary and hence in the sexual cycle and on conception. The anterior pituitary gland has been termed the motor of the ovaries (Aschheim and Zondek).

Physiological Basis for Glandular Administration.

Human pregnancy is characterized by the rapid appearance of the ante-

rior pituitary sex hormones in the placenta, blood and urine, and later by the similar influx of oestrin. These serve as convenient sources for the production of active extracts, and now the various hormones can be obtained in a high degree of purification. The detection of prolan B has been successfully applied by Aschheim and Zondek as a test for pregnancy with over 98% accuracy in a large series of cases.

The clinical use of ovarian extracts has been based on the fact that disorders of the female are often encountered, for which little can be done. It has been reasoned from the favourable results from thyroid therapy that, if the ovary or anterior pituitary gland were not functioning properly, the administration of glandular products from other animals would restore the normal function. Often such products contained a certain amount of thymus, pancreas, adrenal or other glands, and usually a little thyroid. Physiologically the only action such a mixture would have can be traced to the thyroid tissue; it is difficult to imagine any other action clinically.

Of the dried tissue extracts on the market, nearly all have been defatted by acetone and are dispensed in the form of pills. Acetone removes both oestrin and the luteal hormone; hence, these materials cannot be expected to have any value as far as the known ovarian hormones are concerned. Moreover, these dried tissues are taken by mouth; it is found in animal assays that 60—95% of the potency is lost when administered orally.

The early liquid extracts were no better than the dried whole glands. Now, however, several firms put up extracts of oestrin and prolan B for hypodermic use with definitely stated potency. It is by the use of such extracts on carefully studied cases that we may hope to obtain results. No doubt the luteal hormone will also be available clinically. There is an open field for research on both the chemical preparation and clinical application of these products.

There are but two hormones elaborated by the ovary responsible for all the sexual phenomena of the lower mammals, oestrin and the hormone of the corpus luteum. These are in all probability the only ones liberated in the human ovary, and one would expect that any maleffects of the hypofunction of this gland would be relieved by these hormones. The administration of oestrin, or the luteal hormone, either separately or in succession is the basis of any logical ovarian substitution therapy.

A test has been devised by Frank for the occurrence of oestrin in the blood of women. This hormone can be detected in the blood just preceding menstruation. When this pre-menstrual rise is absent it is likely that oestrin would prove of value, but not if the blood already contained large amounts of oestrin. As yet there has not been shown any similar luteal cycle, so that the optimum period for luteal therapy must be gauged from other knowledge. In view of the dual action of the two ovarian hormones in the sex cycles of many lower animals, and probably also in the human, a combination of these might be expected to give the best results in cases of ovarian hypofunction.

In view of the dependence of the ovary on the anterior pituitary gland, it is reasonable that certain types of menstrual disorder may be ascribed to this gland. There may be cases when the ovaries, still capable of normal function, do not receive the required stimulus. Clinical administration of active anterior pituitary preparations in such cases should prove of value. Prolan B, the luteinizing factor, is available in considerable purity, and is active only by injection. Recently Collip has prepared from the placenta a substitute that is physiologically similar to prolan A, the follicle ripening hormone, which he terms emmenin. This material has the great advantage of being active by mouth in very nearly the same potency as by injection. Emmenin and thyroxin stand in sharp contrast to the long list of hormones that

are either not absorbed, or destroyed in the gastro-intestinal tract.

It is thus seen that there are two types of treatment for disorders of the female: (i) Administration of the hormones that are active in the absence or non-function of the ovary, oestrin and the luteal hormone. This includes castration, and degenerative conditions of the ovary. (ii.) Administration of prolan A or prolan B, which only are effective when the ovary is functionally capable of producing its own hormones. In the second group, it is obvious that the same effects could probably be obtained by the administration of the ovarian hormones, but it would seem more physiological if the ovary itself were stimulated to carry out its normal function.

Clinical Trials.

Clinically, glandular therapy with the sex principles of the ovary and anterior pituitary gland have not been very successful. In a great mass of literature on the use of dried extracts the results have been very conflicting, but the majority of workers show no effects for these products. Of recent work on biologically standardized extracts, that of Dodds and Robertson, has been most interesting. Using small doses of oestrin (10 R.U. per day), 40% of 62 cases of functional amenorrhoea showed bleeding. Gardiner-Hill and Smith found negative results in primary amenorrhoea. In secondary amenorrhoea, however, they obtained an improvement in 20 and a restoration of the normal rhythm in 12 out of 37 cases. Hamblen, using oestrin and prolan B (about 56 R. U. of each), obtained favourable results in the menopause and oligomenorrhoea, and was able to initiate bleeding in 9 of 11 cases of primary and secondary amenorrhoea. Zondek uses oestrin in cases of amenorrhoea, disturbances of the cycle, climateric, sterility and habitual abortion. In cases of amenorrhoea he advises combined oestrin and prolan therapy. He also finds prolan of value in excessive bleeding. Campbell and Collip have used both the "pituitary-like hormone of the placenta" (prolan B) and emmenin (prolan A) in a small group of cases. They have some very excellent results in the majority of their trials. Their classification for purposes of treatment is as follows:

i. *Emmenin*—
Menopause of recent origin;
Lengthens cycle in oligo-menorrhoea;
Corrects certain types of amenorrhoea;
Dysmenorrhoea.

ii. *Anterior pituitary-like hormone*—
Menorrhagia;
Metrorrhagia.

In a more recent series of 62 cases in which the amenorrhoeic patients received 20 R.U. of oestrin per day for a month or more, Dodds was able to initiate bleeding in 28. In a good many of the others, while menstruation was not noted, yet favourable psychic results were seen. Dodds states that these have little if any value as criteria of potency of the extracts, because similar results were often observed after injection of normal saline solution.

Novak and Hurd have reported on 51 cases of functional haemorrhage. In 44 of these cases the bleeding was checked by the use of 200 R.U. daily of the lutealizing hormone. This condition is characterized by the presence of ripe follicles in the ovary, but no corpora lutea. The injections of prolan B were made in an attempt to bring about the formation of the yellow body, and initiate the normal cycle.

In short, the conditions that have been investigated and show some indication for the use of the sex hormones are as follows:

i. *Oestrin*—In amenorrhoea, both primary and secondary, at the menopause and possibly in some cases of habitual abortion.

ii. *Prolan B*—Menorrhagia and metrorrhagia.

iii. *Prolan B and Oestrin*—Amenorrhoea (primary and secondary).

iv. *Emmenin (Collip)*—See above.

Besides these uses there are many that show possibilities, but on which little work has been done. That oestrin might be of value in labour is foreshadowed from the fact that oestrin will sensitize the uterus to small doses of pituitrin (Parkes). It is also known that sterility can be brought about in animals by hormone injections. Haberlandt states that in Russia experiments have been successful in the introduction of temporary sterility in women. The use of hormones will also bring about abortion, especially in the early stages of pregnancy, a fact that might have a clinical application if it could be extended to humans.

The results indicated above are sufficient to encourage further work on the therapy of the sex hormones. In view of the rapid excretion by the kidneys this will probably be most efficiently carried out by frequent, small doses. Above all, the success of the treatment depends on correct diagnosis of the disorder; many menstrual disorders are caused by thyroid conditions, malnutrition and debilitation, which must be corrected first. The diagnosis is worthy of the best efforts of the clinician, if sound results are expected.

Conclusions.

Ovarian and pituitary therapy is not a new development in medicine, but rather an old one that has fallen into disrepute. The use of unassayed extracts has led to many abuses in a field that has yet to prove its merit. With the concentrates now being obtained by the physiological chemist an almost untried instrument is placed in the hands of the physician. It is his to accept or reject. It is only by careful study of each case, and with the help of laboratory blood and urine tests for the sex hormones, that the results can be adequately controlled. This is a research worthy of the best combined efforts of the physiologist and the clinician.

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BOOK NOTES

THE McGILL STUDENT JOURNAL

We must begin this discussion with the profound hope that the allusion in the introductory editorial of this new journal to the Biblical gentleman who fell among thieves does not reflect on the character or reputation of brother members of the small band of student medical journals of this continent; and we hasten to assure this youngest brother that not only will we not attempt to strip him of his raiment, but that he will find us willing to co-operate with him in any way within our humble ability, and to help him on any step of this new adventure.

In the same kindly spirit we venture to pen a few impressions gained from the first (November) number, which is at hand.

The first editorial policy mentioned is the intention, in as far as it is possible, to publish in each issue a symposium on some special subject. This idea strikes us as having in it a deal of merit, in that it makes the journal a much readier reference to the student than one which contains random articles on miscellaneous subjects, entailing so often a long and frantic search for material on some particular line — a very trying procedure with an examination imminent and little time to spare.

On one point, however, we find ourselves possessed of some doubt. The editors avow their intention with a "certain amount of pride," to build the journal entirely on the efforts of undergraduates. This we take to mean the barring of all staff contributions. While this undoubtedly will assist in emphasizing one phase of its functions, that is, as a medium of student expression, there is likewise no doubt that it will prevent the publication of many excellent treatises written by experienced men, with the student particularly in mind, which could be found in none of the specialized medical journals. We hope, however, that their confidence in this course, if maintained, will be amply justified.

Of the actual substance of the present number, we might say that we consider the symposium on medical education interesting and valuable as a brief survey of past and current methods in the great medical schools of the world.

As for the case report (for answer turn to page 62), with little shame we admit that it baffled us completely; and we were not alone in our density. We really feel that a case report should not be made into a kind of puzzle or riddle with the solution hidden away in the back of the book — not because we are averse to the sporting element which this method introduces, but because we feel it is not the most helpful manner of presentation.

The article on artificial pneumothorax by Gordon Lynch is excellent in every way and contains more real substance than anything else in the book.

We, personally, could have done without the two humorous efforts; but that, one supposes, is a matter of opinion.

In conclusion, it would be remiss not to mention the splendid printing and binding, especially commending the

fine, large, clear type and good paper, with the hope that this important detail will be always as well maintained. And one parting hope — that these few impressions will be taken in the kindly spirit in which they are intended, and that we will not be considered presumptious in writing them.

So much space have I taken already that there is but little left to mention books. There are, however, two in mind. The first, "Devils, Drugs and Doctors," by Howard W. Haggard, M.D., which is reviewed at length in the McGill Journal, is an account of the superstitions which have through the ages impeded the progress of medical science. It is a vivid and fascinating book, and affords many interesting and little known sidelights on medical history. The book is profusely and uniquely illustrated, and is well worth going through if only for the sake of the illustrations.

On the new bookshelf in the reading-room there is a little volume, "The History of Medicine: A Short Synopsis," by Bernard Dawson, which is recommended to anyone who wishes a brief, well written outline of medical history.

A.

WHAT PRICE AN M.D.?

Many estimates have been ventured by various observers as to the amount of money spent by the average young man —or in many instances no doubt by his parents—in order to provide him with a medical education. The impression has been that the cost is approximately $1,000 a year for tuition and maintenance. The investigation made by Dr. Leland reveals the actual sum spent by the student in any year as $1,100, this including tuition and fees, books and periodicals, board and room, clothing and laundry, and recreation. In 1920, by contrast, the amount was almost $900. The figures submitted do not include the cost of premedical education or such expenses as may be incurred during the term of internship that is desired by most graduates and medical staffs. Neither do the figures take into account the interest on the investment or the amount of money the young man might have earned were he in a gainful occupation rather than in a professional school. At the lowest possible estimate, apparently, a medical education must cost at least $5,000, and, if all the factors are taken into account, may cost in actual cash expended as much as $10,000. If possible earnings and interest are added, the cost may actually reach $20,000. It is doubtful whether there is any other occupation in which men engage in which the cost of training is so great. Certainly there is no other vocation in which the time spent to reach efficiency is so extended. The gradual lengthening of the medical curriculum through the demands for premedical education, for internship and for special training has prolonged the infancy of the young man in medicine to almost thirty years. The human infant at best has the longest period of infancy of any living species. Whereas many animals are competent to take care of themselves and, indeed, to produce families one week after birth, the human infant is not competent to take care of himself until from eighteen to twenty years after birth. If he embarks on a professional vocation, the period is extended to thirty years. From the point of view of the biologist, it is doubtful whether this is a sound trend of human life. The persons most likely to produce progeny capable of raising the intellectual if not the physical standard of the race postpone their maturity beyond the age when biologists are convinced that optimal conditions exist for reproduction.

(From an editorial in the Journal of the American Medical Association.)

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